

REMARKS

A Petition for Extension of Time is being concurrently filed with this Amendment. Thus, this Amendment is being timely filed.

Applicants respectfully request the Examiner to reconsider the present application in view of the foregoing amendments to the claims and the following remarks.

Status of the Claims

Claims 1 and 4-8 are currently pending in the present application. The Office Action is non-final. Claims 2 and 3 were cancelled without prejudice or disclaimer of the subject matter contained therein. Claims 1, 4, 5 and 8 have been amended without prejudice or disclaimer. No new matter has been added by way of the amendments. Support for claim 1 can be found on page 8, lines 10-12, and page 9, lines 3-6, of the present specification. The amendments to claims 4 and 5 correct their respective dependencies. Support for claim 8 can be found at page 13, lines 10-12 of the present specification. Thus, no new matter has been added.

Based upon the above considerations, entry of the present Amendment is respectfully requested.

Issues Under 35 U.S.C. § 112, Second Paragraph, Indefiniteness

Claim 8 stands rejected under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner asserts that claim 8 is incomplete for omitting essential steps. Applicants respectfully traverse.

Although Applicants disagree, in order to further prosecution, Applicants have amended claim 8, without prejudice or disclaimer of the subject matter contained therein, to include an essential separation step for separating the labeled specific binding materials which are not bound with the analyte. Specifically, claim 8 was amended to include the step of “washing away unreacted labeled specific binding material.” Support for claim 8 can be found at page 13, lines 10-12 of the present specification. Applicants submit that the claims particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Applicants respectfully request reconsideration and withdrawal of the present rejection.

Issue Under 35 U.S.C. § 102(b), Anticipation

Claims 1-4, 6 and 8 stand rejected under 35 U.S.C. § 102(b) as anticipated by Josephson *et al.*, U.S. Patent Application Publication No. 2003/0092029 (hereinafter “Josephson”).

The Examiner asserts that Josephson teaches a composition comprising binding moieties linked to a magnetic particle (particles sizes of 0.02 - 0.2 μm) and that the binding moieties cause a specific interaction with a target molecule via a functionalized polymer such as polyethylene glycol (See Office Action dated August 19, 2008 page 3; hereinafter “Office Action”). Applicants have cancelled claims 2-3, without prejudice or disclaimer of the subject matter contained therein, thus obviating the rejection as to these claims. Applicants respectfully traverse as to the remaining claims.

Although Applicants disagree, in order to further prosecution, Applicants have amended claim 1, without prejudice or disclaimer of the subject matter contained therein, to further define the invention. Applicants respectfully submit that presently amended claim 1 is not anticipated

by Josephson. Josephson discloses magnetic beads having a diameter of 0.02 μm to 0.2 μm . The presently amended claim 1 recites magnetic beads having a diameter 0.5 μm to 10 μm , which is outside the range disclosed within Josephson.

Because “a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference,” the cited Josephson reference cannot be a basis for a rejection under § 102(b). *See Verdegall Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Applicants respectfully request reconsideration and withdrawal of the present rejection.

Issues Under 35 U.S.C. § 103(a), Obviousness

Claim 5 and 7 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Josephson, as applied to claims 1-4, 6 and 8, and in view of Foster, U.S. Patent No. 4,444,879 (hereinafter “Foster”) (see Office Action, page 4).

The Examiner admits that Josephson fails to disclose that polyethylene glycol is bound to the magnetic particle via a biotin-avidin complex and packaging the composition into a kit. Further, the Examiner admits that Josephson does not explicitly teach attaching polyethylene glycol to the surface of magnetic particles via biotin-avidin complex.

The Examiner asserts that Josephson teaches a method of immobilizing a polysaccharide to a nanoparticle, wherein such a polysaccharide is used the same way as polyethylene glycol, as a spacer or linker to bind the binding moiety to the nanoparticle.

The Examiner also asserts that Foster teaches packing assay reagents into a kit with instruction.

Therefore, the Examiner concludes that the skilled artisan would be motivated to immobilize polyethylene glycol to the nanoparticle via a biotin-avidin complex as the polysaccharide, and it would have been obvious to pack the reagents used in the assay taught by Josephson into a kit as taught by Foster. Applicants respectfully traverse.

Although Applicants disagree, in order to further prosecution, Applicants have amended claim 1, without prejudice or disclaimer of the subject matter contained therein, to further define the particle size to have a diameter 0.5 μm to 10 μm , and that the spacer is polyalkylene glycol having 50 to 500 repeat units. Support for claim 1 can be found on page 8, lines 10-12, and page 9, lines 3-6, of the present specification.

Graham v. John Deere, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), has provided the controlling framework for an obviousness analysis. A proper analysis under § 103(a) requires consideration of the four *Graham* factors of: determining the scope and content of the prior art; ascertaining the differences between the prior art and the claims that are at issue; resolving the level of ordinary skill in the pertinent art; and evaluating any evidence of secondary considerations (e.g., commercial success; unexpected results). 383 U.S. at 17, 148 USPQ at 467.

M.P.E.P. § 2143 sets forth the guidelines in determining obviousness. But before the Examiner can utilize these guidelines, the Examiner has to take into account the factual inquiries set forth in *Graham v. John Deere; supra*. To reject a claim based on the above mentioned guidelines, the Examiner must resolve the *Graham* factual inquiries. MPEP §2143.

If the Examiner resolves the *Graham* factual inquiries, then the Examiner has to provide some rationale for determining obviousness, wherein M.P.E.P. § 2143 sets forth the rationales that were established in *KSR Int'l Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Applicants respectfully submit that the Examiner has not appropriately resolved the *Graham* factors, including the factors of determining the scope and content of the prior art and ascertaining the differences between the prior art and the claims that are at issue. Based on the following, Applicants maintain that the above mentioned *Graham* factors actually reside in Applicants' favor. Additionally, Applicants submit that since the Examiner did not resolve the *Graham* factors, the rationale the Examiner provides for combining the cited references is improper.

Applicants respectfully submit that the presently claimed invention is distinct from and unobvious over Josephson combined with Foster.

Amended claim 1 relates to a labeled specific binding material (such as labeled secondary antibody), while claim 8 is the method of detecting an analyte (such as antigen) using the labeled specific binding material.

Differences between the invention and the prior art

Applicants submit that claim 1 is not obvious to a person of ordinary skill in the art, because the claimed invention shows an advantageous effect in which the invention described in the cited reference is incapable to show.

In the prior art, magnetic beads having a larger diameter (hereinafter referred as "the larger beads") have been used for a separation/purification process of specific binding materials such as DNA. The magnitude of magnetic signal given by a magnetic bead is proportioned to its volume. That is to say, the larger beads are suitable for highly sensitive detection (see paragraph

[0003] of the present specification) while magnetic beads having smaller diameter referred in Josephson are not.

However, as indicated in the prior art, it has been impossible for the larger beads to detect the analyte with high sensitivity within a practical detecting period since such beads have extremely low rates of the antigen-antibody reaction (see paragraph [0002] of the present specification).

In other words, the reactivity between a secondary antibody fixed at the surface of the larger beads and an antigen is extremely low due to the low mobility and rapid sedimentation of the larger beads having a large weight and size.

Therefore, there are no labeled specific binding materials having high sensitivity which satisfy both a large output signal and high rate of the antigen-antibody reaction.

In contrast, the claimed invention is a labeled specific binding material comprising a substance capable of specifically binding to an analyte, a spacer and the larger beads. The spacer comprising a linear hydrophilic compound (polyalkylene glycol having 50 to 500 repeat units) works for improvement of the reaction rate. Therefore, the claimed invention achieves both a large output signal, as well as a high rate of the antigen-antibody reaction.

Applicants respectfully submit that within the experimental examples of the present specification, labeled specific binding materials having the spacer comprising a linear hydrophilic compound (polyalkylene glycol having 50 to 500 repeat units) show higher sensitivity irrespective of using the larger beads.

For the convenience of the Examiner, Applicants reproduce the data from Tables 1-4 of the present specification, below.

Definitions:

EG = ethylene glycol unit, MW= molecular weight

Results from Example 1 and 2 (2.8 μ m beads)

Spacer: Biotin-PEG-CO₂-NHS (MW=3400 : 68 EG units)
sensitivity 10 ng/ml (Table 1), 10 ng/ml (Table 2)

Spacer : Biotin only (no EG units)
sensitivity 1000 ng/ml (Table 1), 1000 ng/ml (Table 2)

Results from Example 3 and 4 (1.0 μ m beads)

Spacer: Biotin-PEG-CO₂-NHS (MW=3400, 68 EG units)
sensitivity 1 ng/ml (Table 3), 1 ng/ml (Table 4)

Spacer : Biotin-PEG-Maleimide (MW=525, 2 EG units)
sensitivity 10 ng/ml (Table 3), 10 ng/ml (Table 4)

Spacer : Biotin only (no EG units)
sensitivity 10 ng/ml (Table 3) 10 ng/ml (Table 4)

The results within the examples indicate that the spacer described in claimed invention improves the rate of antigen-antibody reaction and is an unexpected advantageous effect.

In light of the above presently amended claims and remarks, because there is no disclosure, teaching, suggestion, reason or rationale provided in the Josephson reference that would allow one of ordinary skill in the art to arrive at the instant invention as claimed, it follows that the same reference is incapable of rendering the instant invention obvious under the provisions of 35 USC § 103(a). Based upon the above, and applying the *Graham factors* analysis test, it is submitted that a *prima facie* case of obviousness has not been established.

Since the present invention is not obvious in light of Josephson, the combination of Josephson and Foster also fails. The secondary reference, Foster, does not cure the deficiencies of Josephson. Therefore, the combinations of Josephson and Foster do not arrive at the present

invention. Based upon the above, and applying the *Graham factors* analysis test, it is submitted that a *prima facie* case of obviousness has not been established for any of the above mentioned claims. Applicants respectfully request reconsideration and subsequent withdrawal of the above rejection.

CONCLUSION

A full and complete response has been made to all issues as cited in the Office Action. Applicants have taken substantial steps in efforts to advance prosecution of the present application. Thus, Applicants respectfully request that a timely Notice of Allowance issue for the present case.

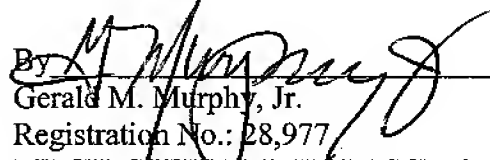
In view of the above remarks, it is believed that claims are allowable.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Paul D. Pyla, Reg. No. 59,228, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: JAN 16 2009

Respectfully submitted,

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